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(54) 【発明の名称】 ヒアルロン酸蓄積促進剤

(57) 【要約】

【課題】 ヒアルロン酸蓄積促進作用を有することから、皮膚しわ改善、皮膚保湿性の増加、皮膚老化防止、血栓形成阻害、関節炎治療、リウマチ治療、ドライアイ治療、血管柔軟化、動脈硬化治療に有効である食品、医薬品及び化粧品を提供すること。

【解決手段】 アロエベラ、ラカンカ、トチュウ、マカ、エンバク、エルカンブリ、カルカデ、ディル、トウキンセンカ、リュウガンニク、フェンネル、チャ、ペニローイヤルミント、ネトル、ピンロウジ、ダッタンソバ、アセンヤク、シクンシ科植物 *Termin7 alia arjuna* から成る群より選ばれる少なくとも1種を含有するヒアルロン酸蓄積促進剤。本発明の剤は、有効成分が天然物であるためその毒性は低い。

## 【特許請求の範囲】

【請求項1】 アロエベラ、ラカンカ、トチュウ、マカ、エンバク、エルカンブリ、カルカデ、ディル、トウキンセンカ、リュウガンニク、フェンネル、チャ、ベニーロイヤルミント、ネトル、ピンロウジ、ダッタンソバ、アセンヤク、シクンシ科植物ターミナリア アルジュナ (*Terminalia arjuna*) から成る群より選ばれる少なくとも1種を含有するヒアルロン酸蓄積促進剤。

【請求項2】 請求項1記載のヒアルロン酸蓄積促進剤を含む皮膚しわ改善用、皮膚保湿用及び／又は皮膚老化予防用組成物。

【請求項3】 請求項1記載のヒアルロン酸蓄積促進剤を含む血栓形成阻害用組成物。

【請求項4】 請求項1記載のヒアルロン酸蓄積促進剤を含む関節炎治療用及び／又はリウマチ治療用組成物。

【請求項5】 請求項1記載のヒアルロン酸蓄積促進剤を含む血管柔軟化用及び／又は動脈硬化治療用組成物。

【請求項6】 請求項1記載のヒアルロン酸蓄積促進剤を含むドライアイ予防用組成物。

【請求項7】 食品である請求項1記載のヒアルロン酸蓄積促進剤又は請求項2～6のいずれか1項記載の組成物。

【請求項8】 化粧品である請求項1記載のヒアルロン酸蓄積促進剤又は請求項2記載の組成物。

【請求項9】 皮膚外用である請求項1記載のヒアルロン酸蓄積促進剤又は請求項2～6のいずれか1項記載の組成物。

【請求項10】 医薬である請求項1記載のヒアルロン酸蓄積促進剤又は請求項2～6のいずれか記載の組成物。

## 【発明の詳細な説明】

## 【0001】

【発明が属する技術分野】本発明は、ヒアルロン酸の蓄積促進作用に関連し、さらに極めて安全性が高い皮膚しわ改善、皮膚保湿性の増加、皮膚老化防止、血栓形成阻害、関節炎治療、リウマチ治療、ドライアイ治療、血管柔軟化、動脈硬化治療などに有効性を示す食品、医薬及び化粧品に関する。

## 【0002】

【従来の技術】ヒアルロン酸は $\beta$ -D-N-アセチルグルコサミンと $\beta$ -D-グルクロン酸が交互に結合した直鎖状の高分子多糖であり、哺乳動物の皮膚、血管、関節、眼球硝子体などの結合組織に広く分布するグリコサミノグルカンの一種である。ヒアルロン酸の各組織での機能としては、その高い水分保持能力、粘弾性や結合性の高さからコラーゲンとともに組織の潤滑性と柔軟性、細胞の保持、外力などの機械的障害への抵抗などに深く関与している。各組織におけるヒアルロン酸の産生量は老化とともに減少し、その結果としてヒアルロン酸が多く存在する皮膚を初めとして、血管、関節、眼球などの

組織で各種の障害や病態が発生すると言われている。また、ヒアルロン酸には、血栓形成阻害作用も報告されており (Artery19(5), 256-270(1992))、その産生量を促進することによって前述の各組織で発生する障害や病態に対する改善作用の他、血液循環系にも改善作用を有することが知られている。

【0003】これまでに皮膚のしわや関節炎など、ヒアルロン酸の減少に伴う各種の障害や疾患に対してヒアルロン酸を直接、外用剤、あるいは注射剤として投与する試みがなされてきた。しかし、ヒアルロン酸は高分子の多糖成分であることから経皮吸収は少なく、さらに注射剤による補完療法は、医師の処方が必要であり、苦痛を伴う治療であることから日常的に使える手法ではない。また、生体内でヒアルロン酸の合成を促進したり (特開平13-163794、特開平13-114637、特開平12-136147)、分解酵素であるヒアルロニダーゼを阻害する技術 (特開平12-178196、特開平11-21247、特開平9-241150)が、これまでに開示されてきた。しかし、効果、安全性、供給、品質、安定性などの面から不十分であり、新規なヒアルロン酸蓄積促進剤の開発が望まれていた。

## 【0004】

【発明が解決しようとする課題】本発明の課題は、ヒアルロン酸合成促進、あるいはヒアルロニダーゼ阻害作用によって各組織でのヒアルロン酸含量を高値に保ち、連用しても副作用の恐れがない、効果的で極めて安全性の高いヒアルロン酸蓄積促進作用を示す組成物およびこれらを含有する食品、医薬、化粧品を提供することにある。

## 【0005】

【課題を解決するための手段】本発明者は、上記目的より鋭意研究を重ねた結果、ある特定の種の植物に高いヒアルロン酸蓄積促進活性を有することを見出し、本発明を完成させた。すなわち、本発明は、アロエベラ、ラカンカ、トチュウ、マカ、エンバク、エルカンブリ、カルカデ、ディル、トウキンセンカ、リュウガンニク、フェンネル、チャ、ベニーロイヤルミント、ネトル、ピンロウジ、ダッタンソバ、アセンヤク及びシクンシ科植物 *Terminalia arjuna* から成る群より選ばれる少なくとも1種を含有するヒアルロン酸蓄積促進剤、該剤を含む皮膚しわ改善用組成物、皮膚保湿用組成物、皮膚老化予防用組成物、血栓形成阻害用組成物、関節炎治療用組成物、リウマチ治療用組成物、ドライアイ予防用組成物、血管柔軟化用組成物、動脈硬化治療用組成物、さらにそれらを含有する食品、医薬及び化粧品に関する。

## 【0006】

【発明の実施の形態】本発明の組成物の有効成分は、アロエベラ (*Aloe vera*)、ラカンカ (*Momordica grosvenori*)、トチュウ (*Eucommia ulmoides*)、マカ (*Lepidium meyenii*)、エンバク (*Avena sativa*)、エルカンブリ (*Centi anella alboracea*)、カルカデ (*Hibiscus sabdariffa*)、

ディル(*Anethum graveolens*)、トウキンセンカ(*Calendula officinalis*)、リュウガンニク(*Euphoria longan* a)、フェンネル(*Foeniculum vulgare*)、チャ(*Thea sinensis*)、ペニーロイヤルミント(*Mentha pulegium*)、ネトル(*Urtrica thunbergiana*)、ビンロウジ(*Areca catechu*)、ダッタンソバ(*Fagopyrum tartaricum*)、アセンヤク(*Uncaria gambir*)、シクンシ科植物ターミナリアアルジュナ(*Terminalia arjuna*)より選ばれる植物である。

【0007】上記植物は、葉、茎、芽、花、木質部、木皮部(樹皮)などの地上部および根、塊茎などの地下部、種子、果実、樹脂など全ての部位が使用可能である。また、植物は、植物自身を乾燥させた乾燥物、その粉碎物、それら自身を圧搾抽出することにより得られる搾汁、水あるいはアルコール、エーテル、アセトンなどの有機溶媒による粗抽出物、および粗抽出物を液液分配、カラムクロマトグラフィーなどで段階的に精製して得られた抽出物画分など、全てを含む。これらは単独で用いても良く、また2種以上混合して用いても良い。

【0008】例えば、リュウガンニクの植物体乾燥物1kgにエタノール3Lを加え、室温で一晩浸漬することにより得た抽出液を、そのままヒアルロン酸蓄積促進作用を有する皮膚しわ改善用組成物、皮膚保湿用組成物、皮膚老化予防用組成物、血栓形成阻害用組成物、関節炎治療用組成物、リウマチ治療用組成物、ドライアイ予防用組成物、血管柔軟化用組成物、動脈硬化治療用組成物として使用しても良いし、液液分配、各種クロマトグラフィーを組み合わせて、精製したものを使用しても良い。

【0009】前記の特定の植物の乾燥物または抽出物がヒアルロン酸蓄積促進作用を有することは、従来から全く知られておらず、本発明により得られた新知見である。ヒアルロン酸は、極めて高い保水能力や粘弾性を示す生体成分として知られている。ヒアルロン酸は生体中では単独で存在することはほとんどないといっており、様々なヒアルロン酸結合活性を有するプロテインなどのヒアルロン酸結合分子が結合して特異なマトリックスを構築している。このヒアルロン酸リッチマトリックスは、活発な代謝変化、細胞増殖がみられる部位にはほとんどにおいて見出されるものである。

【0010】ヒアルロン酸は、その優れた保水能力によって、皮膚の乾燥を防ぎ、みずみずしい肌を保つために使用できる。皮膚はヒアルロン酸を豊富に有する組織であるが、ヒアルロン酸は、加齢とともに低分子化されて、その保水能力が低下していく。そこで、皮膚のヒアルロン酸を豊富に保持することによって、皮膚の老化を防止することができる。

【0011】ヒアルロン酸の産生量を促進することによって、ヒアルロン酸の産生量の減少により生じる血管、関節、眼球などの組織で発生する障害や病態を改善することができる。また、血栓形成阻害作用を有しているヒアルロン酸の産生を促進することにより、血栓形成を阻

害することができる。

【0012】本発明の剤は、ヒアルロン酸蓄積作用を有し、皮膚しわ改善用組成物、皮膚保湿用組成物、皮膚老化予防用組成物、血栓形成阻害用組成物、関節炎治療用組成物、リウマチ治療用組成物、ドライアイ予防用組成物、血管柔軟化用組成物、動脈硬化治療用組成物、ならびにこれらを含む食品、医薬及び化粧品として使用可能である。

【0013】本発明の剤を使用して、皮膚しわ改善用組成物、皮膚保湿用組成物、皮膚老化予防用組成物、血栓形成阻害用組成物、関節炎治療用組成物、リウマチ治療用組成物、ドライアイ予防用組成物、血管柔軟化用組成物、動脈硬化治療用組成物、ならびにこれらを含む食品、医薬、化粧品を製造することができる。

【0014】本発明の皮膚しわ改善用組成物、皮膚保湿用組成物、皮膚老化予防用組成物、血栓形成阻害用組成物、関節炎治療用組成物、リウマチ治療用組成物、ドライアイ予防用組成物、血管柔軟化用組成物、動脈硬化治療用組成物は、適宜食品、医薬、化粧品として適用することができる。医薬としての適用では、経口投与又は非経口投与のいずれも採用することができる。医薬としての投与に際しては、有効成分を経口投与、経皮投与、直腸内投与、注射などの投与方法に適した固体又は液体の医薬用無毒性担体と混合して、慣用の医薬製剤の形態で投与することができる。このような製剤としては、例えば、錠剤、顆粒剤、散剤、カプセル剤などの固形剤、溶液剤、懸濁剤、乳剤などの液剤、凍結乾燥製剤などが挙げられ、これらの製剤は製剤上の常套手段により調製することができる。上記の医薬用無毒性担体としては、例えば、グルコース、乳糖、ショ糖、澱粉、マンニトール、デキストリン、脂肪酸グリセリド、ポリエチレングリコール、ヒドロキシエチルデンプン、エチレングリコール、ポリオキシエチレンソルビタン脂肪酸エステル、アミノ酸、ゼラチン、アルブミン、水、生理食塩水などが挙げられる。また、必要に応じて、安定化剤、湿潤剤、乳化剤、結合剤、等張化剤などの慣用の添加剤を適宜添加することもできる。

【0015】食品としては、そのまま、又は種々の栄養成分を加えて、若しくは飲食品中に含有せしめて、皮膚しわ改善剤、皮膚保湿剤、皮膚老化予防剤、血栓形成阻害剤、関節炎治療剤、リウマチ治療剤、ドライアイ予防剤、血管柔軟化剤、動脈硬化治療剤に有用な保健用食品又は食品素材として食することができる。例えば、上述した適当な助剤を添加した後、慣用の手段を用いて、食用に適した形態、例えば、顆粒状、粒状、錠剤、カプセル、ペーストなどに成形して食用に供してもよく、また種々の食品、例えば、ハム、ソーセージなどの食肉加工食品、かまぼこ、ちくわなどの水産加工食品、パン、菓子、バター、粉乳、発酵乳製品に添加して使用したり、水、果汁、牛乳、清涼飲料、茶などの飲料に添加して使

用してもよい。

【0016】本発明において、有効成分たる植物の有効投与量は、患者の年齢、体重、症状、患者の程度、投与経路、投与スケジュール、製剤形態、素材の阻害活性の強さなどにより、適宜選択・決定されるが、例えば、経口投与の場合、一般に1日当たり0.001~1000mg/kg程度、アロエベラのエタノール抽出物の場合、1日当たり10~200mg/kg程度とされ、1日に数回に分けて投与してもよい。

【0017】また、本発明の剤を含有せしめて、ヒアルロン酸蓄積促進剤含有化粧品または化粧品素材として使用する場合、例えば、エンバクの乾燥物あるいは抽出物を小麦胚芽油あるいはオリーブ油に添加して化粧品素材として使用することができる。本発明における植物の乾燥物または抽出物の添加量は、特に限定されるものではないが、一例としてあげると、小麦胚芽油あるいはオリーブ油の重量に対して0.1重量%以上60重量%以下、好ましくは、0.5重量%以上50重量%以下が適当である。

【0018】また、前記のヒアルロン酸蓄積促進剤を直接、化粧品成分として使用した化粧品を製造することができる。本発明の方法で得られるヒアルロン酸蓄積促進剤を含有せしめた化粧品としては特に限定されるものではないが、機能面からは、例えば乳液、化粧液、フェイスクリーム、ハンドクリーム、ローション、エッセンス、シャンプー、リンスなどが好ましい。このような化粧品は、常法に従って製造することができる。化粧品における有効成分である植物の乾燥物または抽出物の添加量は、特に限定されるものではないが、一例としてあげると、化粧品全重量の0.01重量%以上20重量%以下程度が適当である。

【0019】本発明の有効成分である植物は、天然物であるためその毒性は低く、例えばフェネルのエタノール抽出物を毎日1000mg/kg、100日間という長期間に亘ってラットに経口投与しても、死亡例は認められず、体重変化も観察されなかった。

【0020】

【実施例】以下に実施例を挙げて、具体的に説明する

が、本発明はこれらに限定されるものではない。

実施例1~17

【植物の抽出】アロエベラ、ラカンカ、トチュウ、マカ、エンバク、エルカンブリ、カルカデ、ディル、トウキンセンカ、リュウガンニク、フェネル、チャ、ベニーロイヤルミント、ネトル、ピンロウジ、ダッタンソバ、アセンヤク、シクンシ科植物 *Terminalia arjuna*、各20gにエタノール100mLを加え、50°C、1500P.S.I.で20分間、加熱抽出した後、エタノールを留去した。各エタノール抽出乾燥物としてそれぞれ上記記載順に、1350、3760、3980、1670、1090、2340、2100、2870、3850、3210、3990、2860、3460、2650、2850、1890、3560、2870mgを得た。

【0021】【薬理試験】

ヒアルロン酸蓄積促進試験

ヒアルロン酸蓄積促進作用はホルマリン固定赤血球懸濁液を用いた試験(生化学73(2),429-438(2001))を参考にし、その改良法を構築して評価した。すなわち、ヒト繊維芽細胞を組織培養用プレートで培養させたのち、上記で調製した植物エキスを5mg/mLの濃度で16時間作用させた。培地を除去したのち、2.3mg/mLの濃度の陰イオン性コロイド粒子懸濁液50・L(ホルベン社、843 PERMANENT GREEN DEEP)を添加し、細胞のヒアルロン酸リッチマトリックスによって排除された領域を顕微鏡下で観察して目視的に活性を判定した。各植物エキスのヒアルロン酸蓄積促進作用に対する評価結果を表1に示した。なお、判定基準は□=排除面積が若干増加、○=増加、◎=顕著に増加で表した。

【0022】表1で示したように、本発明の植物であるアロエベラ、ラカンカ、トチュウ、マカ、エンバク、エルカンブリ、カルカデ、ディル、トウキンセンカ、リュウガンニク、フェネル、チャ、ベニーロイヤルミント、ネトル、ピンロウジ、ダッタンソバ、アセンヤク、シクンシ科植物 *Terminalia arjuna*はヒアルロン酸蓄積促進作用を示すことがわかる。

【0023】

【表1】

表1. 各エタノール抽出エキスのヒアルロン酸蓄積促進作用

	和 名	学 名	作 用
実施例1	アロエベラ	<i>Aloe vera</i>	◎
実施例2	ラカンカ	<i>Momordica grosvenorii</i>	□
実施例3	トチュウ	<i>Eucommia ulmoides</i>	○
実施例3	マカ	<i>Lepidium meyenii</i>	□
実施例4	エンバク	<i>Avena sativa</i>	□
実施例5	エルカンブリ	<i>Gentiana alba</i>	□
実施例6	カルカデ	<i>Hibiscus sabdariffa</i>	□
実施例7	ディル	<i>Anethum graveolens</i>	□
実施例8	トウキンセンカ	<i>Calendula officinalis</i>	□
実施例9	リュウガンニク	<i>Euphorbia longana</i>	◎
実施例10	フェンネル	<i>Foeniculum vulgare</i>	○
実施例11	チャ	<i>Thea sinensis</i>	□
実施例12	ペニーロイヤルミント	<i>Mentha pulegium</i>	○
実施例13	ネトル	<i>Urtica thunbergiana</i>	□
実施例14	ビンロウジ	<i>Areca catechu</i>	□
実施例15	ダッタンソバ	<i>Fagopyrum tartaricum</i>	○
実施例16	アセンヤク	<i>Uncaria gambir</i>	□
実施例17	シクンシ科植物	<i>Terminalia arjuna</i>	□

## 【0024】処方例1

〔錠剤の製造〕実施例13で得られたネトルのエタノール\*

(組 成)

ネトル抽出物

乳糖

コーンスターチ

グァーガム

(配合：重量%)

24

63

12

1

\* エタノール抽出を用いて、常法に従って、下記の組成の錠剤を製造した。

## 【0025】処方例2

〔ジュースの製造〕実施例2で得られたラカンカのエタノール\*

(組 成)

冷凍濃縮温州みかん果汁

果糖ブドウ糖液糖

クエン酸

L-アスコルビン酸

香料

色素

ラカンカ抽出物

水

(配合：重量%)

5.0

11.0

0.2

0.02

0.2

0.1

0.2

83.28

\* エタノール抽出物を用いて、常法に従って、下記の組成のジュースを製造した。

## 【0026】処方例3

〔フェイスクリームの製造〕実施例6で得られたカルカデ★

(組 成)

イソステアリン酸イソプロピル

ホホバ油

セタノール

ステアリルアルコール

ポリオキシエチレン라우リルエーテル

プロピレングリコール

(配合：重量%)

8.0

6.0

8.0

2.0

1.5

6.0

★のエタノール抽出物を用いて、常法に従って、下記の組成のフェイスクリームを製造した。

(6)

特開2003-238432

9

10

ソルビトール	1.0
バラベン	0.4
カルカデ抽出物	0.5
ビタミンE	0.5
香料	0.1
精製水	66.0

【0027】

【発明の効果】本発明の植物は、ヒアルロン酸蓄積促進作用を有する皮膚しわ改善、皮膚保湿性の増加、皮膚老\*

\*化防止、血栓形成阻害、関節炎治療、リウマチ治療、ドライアイ治療、血管柔軟化、動脈硬化治療に有効である。

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AC122 AC132 AC182 AC352

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4C088 AB12 AB19 AB26 AB38 AB40

AB43 AB45 AB59 AB75 AB86

AC03 AC04 AC05 AC06 AC08

AC11 AC13 BA09 BA10 MA63

NA14 ZA33 ZA45 ZA54 ZA89

ZA96 ZC02

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CLAIMS

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[Claim(s)]

[Claim 1] Department of aloe vera, RAKANKA, TOCHUU, MAKKA, oats, ERUKAMBURI, Karkade, dill, Calendula officinalis, RYUUGANNIKU, fennel, tea, peignee royal mint, NETORU, areca, buckwheat, cube gambir, and Combretaceae vegetable TAMINARIA Hyaluronic acid are recording accelerator containing at least one sort chosen from the group which consists of Arjuna (Terminalia arjuna).

[Claim 2] The object for a skin wrinkling improvement, the object for skin moisturization, and/or the constituent for skin aging prevention containing a hyaluronic acid are recording accelerator according to claim 1.

[Claim 3] The constituent for thrombosis inhibition containing a hyaluronic acid are recording accelerator according to claim 1.

[Claim 4] The object for an arthritis therapy and/or the constituent for a rheumatism therapy containing a hyaluronic acid are recording accelerator according to claim 1.

[Claim 5] The object for the formation of blood vessel flexible and/or the constituent for an arteriosclerosis therapy containing a hyaluronic acid are recording accelerator according to claim 1.

[Claim 6] The constituent for dry eye prevention containing a hyaluronic acid are recording accelerator according to claim 1.

[Claim 7] The hyaluronic acid are recording accelerator according to claim 1 which is food, or the constituent of claim 2-6 given in any 1 term.

[Claim 8] The hyaluronic acid are recording accelerator according to claim 1 which is cosmetics, or a constituent according to claim 2.

[Claim 9] The hyaluronic acid are recording accelerator according to claim 1 which is skin external use, or the constituent of claim 2-6 given in any 1 term.

[Claim 10] The hyaluronic acid are recording accelerator according to claim 1 which is a remedy, or claims 2-6 are the constituent of a publication either.

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[Translation done.]

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## DETAILED DESCRIPTION

---

[Detailed Description of the Invention]

[0001]

[The technical field to which invention belongs] This invention relates to the food, the remedy, and cosmetics which show effectiveness to the skin wrinkling improvement with safety high further very, the increment in skin moistness, skin aging prevention, thrombosis inhibition, an arthritis therapy, a rheumatism therapy, a dry eye therapy, the formation of blood vessel flexible, an arteriosclerosis therapy, etc. in relation to an are recording acceleration operation of hyaluronic acid.

[0002]

[Description of the Prior Art] Hyaluronic acid is a kind of the GURIKOSAMINO glucan with which beta-D-N-acetylglucosamine and beta-D-glucuronic acid are the macromolecule polysaccharides of the shape of a straight chain combined by turns, and are widely distributed over connective tissue, such as the skin of mammalian, a blood vessel, a joint, and an eyeball vitreous body. As a function in each organization of hyaluronic acid, it is participating in the resistance to mechanical failures, such as maintenance of the lubricity of an organization, flexibility, and a cell, and external force, etc. deeply with the collagen from the height of the high moisture maintenance capacity, viscoelasticity, or affinity. The amount of production of the hyaluronic acid in each organization decreases with aging, makes the start the skin in which hyaluronic acid exists mostly as the result, and it is said that various kinds of failures and symptoms in an organization of a blood vessel, a joint, an eyeball, etc. occur. Moreover, thrombosis inhibitory action is also reported to hyaluronic acid (Artery19 (5), 256-270 (1992)), and having an improvement operation also in the blood circulatory system besides to the failure and symptoms which are generated in each above-mentioned organization an improvement operation is known by promoting the amount of production.

[0003] The attempt which prescribes hyaluronic acid for the patient as external preparations or injections directly to various kinds of failures and diseases accompanying reduction of hyaluronic acid, such as a wrinkling, arthritis, etc. of the skin, has so far been made. However, since hyaluronic acid is the polysaccharide component of a macromolecule, there is little percutaneous absorption, a formula of a medical practitioner is still more nearly required for the substitution therapy by injections, and it is not the technique which can be daily used from it being a therapy accompanied by pain. Moreover, composition of hyaluronic acid is promoted in the living body, or the technique (JP,12-178196,A, JP,11-21247,A, JP,9-241150,A) which checks the hyaluronidase which are (JP,13-163794,A, JP,13-114637,A, JP,12-136147,A), and a dialytic ferment has so far been indicated. However, it is inadequate from fields, such as effectiveness, safety, supply, quality, and stability, and development of a new hyaluronic acid are recording accelerator was desired.

[0004]

[Problem(s) to be Solved by the Invention] Even if the technical problem of this invention maintains the hyaluronic acid content in each organization at a high price and uses it continuously by the acceleration of hyaluronic acid composition, or hyaluronidase inhibitory action, it is to offer the food containing the constituent and these without fear of a side effect which are effective and show the hyaluronic acid are recording acceleration operation with very high safety, a remedy, and cosmetics.

[0005]

[Means for Solving the Problem] this invention person made a certain specific kind of vegetation complete a header and this invention for having high hyaluronic acid are recording acceleration activity, as a result of repeating research wholeheartedly from the above-mentioned object. This invention Namely, an aloe vera, RAKANKA, TOCHUU, MAKKA, oats, ERUKAMBURI, Karkade, a dill, Calendula officinalis, RYUUGANNIKU, A fennel,



tea, a peignee royal mint, NETORU, areca, a buckwheat, Cube gambir and department vegetation of Combretaceae. The hyaluronic acid are recording accelerator containing at least one sort chosen from the group which consists of Terminalia arjuna, The constituent for a skin wrinkling improvement containing this \*\*, the constituent for skin moisturization, the constituent for skin aging prevention, It is related with the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye \*\*\*\*\*, the constituent for the formation of blood vessel flexible, the constituent for an arteriosclerosis therapy, the food that contains them further, a remedy, and cosmetics.

[0006]

[Embodiment of the Invention] The active principle of the constituent of this invention An aloe vera (Aloe vera), RAKANKA (Momordica grosvenorii), TOCHUU (Eucommia ulmoides), MAKU (Lepidium yunnanense), oats (Avena sativa), ERUKAMBURI (Gentiana alba), Karkade (Hibiscus sabdariffa), A dill (Anethum graveolens), Calendula officinalis (Calendula officinalis), RYUUGANNIKU (Euphorbia longana), a fennel (Foeniculum vulgare), Tea (Thea sinensis), a peignee royal mint (Mentha pulegium), NETORU (Uraria thunbergiana), areca (Areca catechu), They are a buckwheat (Fagopyrum tartaricum), cube gambir (Uncaria gambir), and the vegetation chosen from department of Combretaceae vegetable TAMI nari R JUNA (Terminalia arjuna).

[0007] All parts of the above-mentioned vegetation, such as the roots, such as terrestrial parts, such as a leaf, a stem, a bud, a flower, cignin, and the bark section (bark), and a root, and a tuber, a seed, fruits, and resin, are usable. Moreover, vegetation contains all for the extract fraction which refined gradually the crude extract by organic solvents, such as the dry matter which dried the vegetation itself, its grinding object, juice obtained by carrying out the squeezing extract of these selves, water or alcohol, the ether, and an acetone, and the crude extract with liquid-liquid distribution, a column chromatography, etc., and was obtained. These may be used independently, and two or more sorts may be mixed and they may be used.

[0008] For example, ethanol 3L is added to 1kg of plant body dry matters of RYUUGANNIKU. The constituent for a skin wrinkling improvement which has a hyaluronic acid are recording acceleration operation for the extract obtained by being immersed at a room temperature overnight as it is, The constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, You may use it as the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, and a constituent for an arteriosclerosis therapy, and the refined thing may be used combining liquid-liquid distribution and various chromatographies.

[0009] That a specific aforementioned vegetable dry matter or an aforementioned specific vegetable extract has a hyaluronic acid are recording acceleration operation is the new knowledge which was not known at all from the former but was acquired by this invention. Hyaluronic acid is known as a biogenic substance which shows very high water retention capacity and viscoelasticity. You may say that hyaluronic acid does not almost have existing independently in a living body, hyaluronic acid tie molecules, such as a protein which has various hyaluronic acid avidity, join together, and the unique matrix is built. This hyaluronic acid rich matrix is found out in most by the part to which an active metabolic turnover change and cell proliferation are seen.

[0010] Hyaluronic acid can be used in order to prevent desiccation of the skin and to maintain the fresh skin according to the outstanding water retention capacity. Although the skin is an organization which has hyaluronic acid in abundance, depolymerize of the hyaluronic acid is carried out with aging, and the water retention capacity declines. Then, aging of the skin can be prevented by holding the hyaluronic acid of the skin to abundance.

[0011] By promoting the amount of production of hyaluronic acid, the failure and symptoms which are generated in the organization of the blood vessel produced by reduction of the amount of production of hyaluronic acid, a joint, an eyeball, etc. are improvable. Moreover, thrombosis can be checked by promoting the production of hyaluronic acid which has thrombosis inhibitory action.

[0012] \*\* of this invention has hyaluronic acid cumulation, and is usable as the constituent for a skin wrinkling improvement, the constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, the constituent for an arteriosclerosis therapy and the food containing these, a remedy, and cosmetics.

[0013] \*\* of this invention can be used and the constituent for a skin wrinkling improvement, the constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, the constituent for an arteriosclerosis therapy and the food containing these, a remedy, and cosmetics can be manufactured.

[0014] The constituent for a skin wrinkling improvement of this invention, the constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, and the constituent for an arteriosclerosis therapy are applicable as food, a remedy, and cosmetics suitably. In the application as a remedy, either internal use or parenteral administration is employable. An active principle can be mixed with the avirulent support for remedies of the solid-state suitable for medication methods, such as internal use, dermal administration, intrarectal administration, and injection, or a liquid on the occasion of the administration as a remedy, and a medicine can be prescribed for the patient with the gestalt of the remedy pharmaceutical preparation of common use. As such pharmaceutical preparation, liquids and solutions, such as solid preparations, such as a tablet, a granule, powder, and a capsule, a solution agent, suspension, and an emulsion, lyophilized products, etc. are mentioned, and these pharmaceutical preparation can be prepared by the stock-in-trade on pharmaceutical preparation, for example. As the above-mentioned avirulent support for remedies, a glucose, a lactose, cane sugar, starch, a mannitol, a dextrin, a fatty-acid glyceride, polyethylene glucohol, hydroxyethylated starch, ethylene glycol, polyoxyethylene sorbitan fatty acid ester, amino acid, gelatin, albumin, water, a physiological saline, etc. are mentioned, for example. Moreover, additives of common use, such as a stabilizing agent, a wetting agent, an emulsifier, a binder, and an isotoning agent, can also be added suitably if needed.

[0015] As food, you add nutrition components remaining as it is or various, or make it contain in an eating-and-drinking article, and it can eat as the useful food for health, or a food raw material to a skin wrinkling improvement agent, a skin moisturizer, skin aging preventive, a thrombosis inhibitor, an arthritis therapy agent, a rheumatism therapy agent, dry eye preventive, a blood vessel flexible-sized agent, and an arteriosclerosis therapy agent. For example, the gestalt which was suitable for edible using the means of common use after adding the suitable assistant mentioned above, For example, it may fabricate to granularity, a grain, a tablet, a capsule, a paste, etc., and you may present edible. Moreover, it may be added and used for seafood processing food, such as meat-processing food, such as various food, for example, a hum, and a sausage, boiled fish paste, and a fishcake tube, a pan, confectionery, butter, milk powder, and a fermented milk product, or you may add and use it for drinks, such as water, fruit juice, cow's milk, a soft drink, and tea.

[0016] Although it sets to this invention and the effective dose of active principle slack vegetation is suitably chosen and determined by the strength of a patient's age, weight, a symptom, a patient's extent, a route of administration, an administration schedule, formulation, and the inhibition activity of a raw material etc. For example, in internal use, in the case of per [ 0.001 ] day - 1000 mg/kg extent, and the ethanol extract of an aloe vera, generally, it considers per [ 10 ] day - as 200 mg/kg extent, and a medicine may be prescribed for the patient in several steps on the 1st.

[0017] Moreover, when making \*\* of this invention contain and using it as hyaluronic acid are recording accelerator content cosmetics or a cosmetics raw material, the dry matter or extract of oats can be added in a wheat germ oil or olive oil, and it can be used as a cosmetics raw material. If especially the addition of the dry matter of the vegetation in this invention or an extract is raised as an example, 50 or less % of the weight 0.5 % of the weight or more is suitable for it, although it is not limited 60 or less % of the weight 0.1 % of the weight or more preferably to the weight of a wheat germ oil or olive oil.

[0018] Moreover, the cosmetics which used the aforementioned hyaluronic acid are recording accelerator as a cosmetics component directly can be manufactured. Although not limited especially as cosmetics which made the hyaluronic acid are recording accelerator obtained by the approach of this invention contain, from a functional side, a milky lotion, makeup liquid, a face cream, a hand cream, a lotion, essence, a shampoo, a rinse, etc. are desirable. Such cosmetics can be manufactured according to a conventional method. Although it is not limited, if especially the addition of the dry matter of the vegetation which is an active principle in cosmetics, or an extract is raised as an example, 0.01-% of the weight or more 20 or less % of the weight extent of all cosmetics weight is suitable for it.

[0019] Since the vegetation which is the active principle of this invention was a natural product, even if the toxicity was low, for example, it continued every day at the long period of time of 1000 mg/kg and 100 days and administered the ethanol extract of a fennel orally to the rat, the example of death was not accepted and weight change was not observed, either.

[0020]

[Example] Although an example is given to below and explained concretely, this invention is not limited to these. An examples 1-17 [vegetable extract] aloe vera, RAKANKA, TOCHUU, MAKAKA, oats, ERUKAMBURI, Karkade, a

dill, Calendula officinalis, RYUUGANNIKU, a fennel, tea, a peignee royal mint, NETORU, areca, a buckwheat, cube gambir, department vegetation of Combretaceae Ethanol 100mL was added to Terminalia arjuna and 20g each, and ethanol was distilled off after carrying out a heating extract for 20 minutes by 50 degrees C and 1500P.S.I. 1350, 3760, 3980, 1670, 1090, 2340, 2100, 2870, 3850, 3210, 3990, 2860, 3460, 2650, 2850, 1890, and 3560 or 2870mg were obtained in order of [ above-mentioned ] the publication as each ethanol extract dry matter, respectively.

#### [0021] [Pharmacological test]

The hyaluronic acid are recording accelerated test hyaluronic acid are recording acceleration operation referred to the trial (biochemistry 73 (2), 429-438 (2001)) which used formalin fixation erythrocyte suspension, and built and evaluated the improving method. That is, after making Homo sapiens fibrocyte cultivate on the plate for tissue culture, the vegetable extract prepared by the above was made to act by the concentration of 5 mg/mL for 16 hours. After removing a culture medium, anion nature colloidal particle suspension 50 and L of the concentration of 2.3 mg/mL (HORUBEN, 843 PERMANENT GREEN DEEP) were added, the field eliminated by the hyaluronic acid rich matrix of a cell was observed under the microscope, and activity was judged in viewing. The assessment result of a hyaluronic acid are recording acceleration operation of each vegetable extract was shown in a table 1. in addition, a criterion -- \*\*= abatement area -- some -- an increment, the increment in O=, and O= -- it expressed with the increment notably.

[0022] The aloe vera which is the vegetation of this invention as a table 1 showed, RAKANKA, TOCHUU, MAKKA, oats, ERUKAMBURI, Karkade, a dill, Calendula officinalis, RYUUGANNIKU, a fennel, tea, a peignee royal mint, NETORU, areca, a buckwheat, cube gambir, department vegetation of Combretaceae It turns out that Terminalia arjuna shows a hyaluronic acid are recording acceleration operation.

#### [0023]

##### [A table 1]

表1. 各エタノール抽出エキスのヒアルロン酸蓄積促進作用

	和 名	学 名	作 用
実施例 1	アロエベラ	Aloe vera	◎
実施例 2	ラカンカ	Momordica grosvenorii	□
実施例 3	トチュウ	Eucommia ulmoides	○
実施例 3	マカ	Lepidiummee yenii	□
実施例 4	エンバク	Avena sativa	□
実施例 5	エルカンブリ	Gentianella alboroccea	□
実施例 6	カルカデ	Hibiscus sabdariffa	□
実施例 7	ディル	Anethum graveolenns	□
実施例 8	トウキンセンカ	Calendula officinalis	□
実施例 9	リュウガンニク	Euphoria longana	◎
実施例 10	フェンネル	Foeniculum vulgare	○
実施例 11	チャ	Thea sinensis	□
実施例 12	ペニーロイヤルミント	Mentha pulegium	○
実施例 13	ネトル	Urtrica thunbergiana	□
実施例 14	ピンロウジ	Areca catechu	□
実施例 15	ダッタンソバ	Fagopyrum tartaricum	○
実施例 16	アセンヤク	Uncaria gambir	□
実施例 17	シクンシ科植物	Terminalia arjuna	□

[0024] According to the conventional method, the tablet of the following presentation was manufactured using the ethanol extract of NETORU obtained in the example 1 [manufacture of tablet] example 13 of a formula.

(Group \*\*) (combination: % of the weight)

NETORU extract 24 Lactose 63 Corn starch 12 Cyamoposis Gum 1 [0025] According to the conventional method, the juice of the following presentation was manufactured using the ethanol extract of RAKANKA

obtained in the example 2 [manufacture of juice] example 2 of a formula.

(Group \*\*) (combination: % of the weight)

Frozen concentration Wenzhou mandarin orange fruit juice 5.0 Fruit-sugar grape-sugar liquid sugar 11.0 A citric acid 0.2 L-ascorbic acid 0.02 Perfume 0.2 Coloring matter 0.1 RAKANKA extract 0.2 Water 83.28 [0026]

According to the conventional method, the face cream of the following presentation was manufactured using the ethanol extract of Karkade obtained in the example 3 [manufacture of face cream] example 6 of a formula.

(Group \*\*) (combination: % of the weight)

Isostearic acid isopropyl 8.0 Jojoba oil 6.0 Cetanol 8.0 Stearyl alcohol 2.0 The polyoxyethylene lauryl ether 1.5 Propylene glycol 6.0 Sorbitol 1.0 paraben 0.4 Karkade extract 0.5 vitamin E 0.5 Perfume 0.1 purified water 66.0 [0027]

[Effect of the Invention] The vegetation of this invention is effective in the skin wrinkling improvement which has a hyaluronic acid are recording acceleration operation, the increment in skin moistness, skin aging prevention, thrombosis inhibition, an arthritis therapy, a rheumatism therapy, a dry eye therapy, the formation of blood vessel flexible, and an arteriosclerosis therapy.

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[Translation done.]

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**DETAILED DESCRIPTION**

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[Detailed Description of the Invention]

[0001]

[The technical field to which invention belongs] This invention relates to the food, the remedy, and cosmetics which show effectiveness to the skin wrinkling improvement with safety high further very, the increment in skin moistness, skin aging prevention, thrombosis inhibition, an arthritis therapy, a rheumatism therapy, a dry eye therapy, the formation of blood vessel flexible, an arteriosclerosis therapy, etc. in relation to an are recording acceleration operation of hyaluronic acid.

[0002]

[Description of the Prior Art] Hyaluronic acid is a kind of the GURIKOSAMINO glucan with which beta-D-N-acetylglucosamine and beta-D-glucuronic acid are the macromolecule polysaccharides of the shape of a straight chain combined by turns, and are widely distributed over connective tissue, such as the skin of mammalian, a blood vessel, a joint, and an eyeball vitreous body. As a function in each organization of hyaluronic acid, it is participating in the resistance to mechanical failures, such as maintenance of the lubricity of an organization, flexibility, and a cell, and external force, etc. deeply with the collagen from the height of the high moisture maintenance capacity, viscoelasticity, or affinity. The amount of production of the hyaluronic acid in each organization decreases with aging, makes the start the skin in which hyaluronic acid exists mostly as the result, and it is said that various kinds of failures and symptoms in an organization of a blood vessel, a joint, an eyeball, etc. occur. Moreover, thrombosis inhibitory action is also reported to hyaluronic acid (Artery19 (5), 256-270 (1992)), and having an improvement operation also in the blood circulatory system besides to the failure and symptoms which are generated in each above-mentioned organization an improvement operation is known by promoting the amount of production.

[0003] The attempt which prescribes hyaluronic acid for the patient as external preparations or injections directly to various kinds of failures and diseases accompanying reduction of hyaluronic acid, such as a wrinkling, arthritis, etc. of the skin, has so far been made. However, since hyaluronic acid is the polysaccharide component of a macromolecule, there is little percutaneous absorption, a formula of a medical practitioner is still more nearly required for the substitution therapy by injections, and it is not the technique which can be daily used from it being a therapy accompanied by pain. Moreover, composition of hyaluronic acid is promoted in the living body, or the technique (JP,12-178196,A, JP,11-21247,A, JP,9-241150,A) which checks the hyaluronidase which are (JP,13-163794,A, JP,13-114637,A, JP,12-136147,A), and a dialytic ferment has so far been indicated. However, it is inadequate from fields, such as effectiveness, safety, supply, quality, and stability, and development of a new hyaluronic acid are recording accelerator was desired.

[0004]

[Problem(s) to be Solved by the Invention] Even if the technical problem of this invention maintains the hyaluronic acid content in each organization at a high price and uses it continuously by the acceleration of hyaluronic acid composition, or hyaluronidase inhibitory action, it is to offer the food containing the constituent and these without fear of a side effect which are effective and show the hyaluronic acid are recording acceleration operation with very high safety, a remedy, and cosmetics.

[0005]

[Means for Solving the Problem] this invention person made a certain specific kind of vegetation complete a header and this invention for having high hyaluronic acid are recording acceleration activity, as a result of repeating research wholeheartedly from the above-mentioned object. This invention Namely, an aloe vera, RAKANKA, TOCHUU, MAKKA, oats, ERUKAMBURI, Karkade, a dill, Calendula officinalis, RYUUGANNIKU, A fennel,

tea, a peignee royal mint, NETORU, areca; a buckwheat, Cube gambir and department vegetation of Combretaceae The hyaluronic acid are recording accelerator containing at least one sort chosen from the group which consists of Terminalia arjuna, The constituent for a skin wrinkling improvement containing this \*\*, the constituent for skin moisturization, the constituent for skin aging prevention, It is related with the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye \*\*\*\*\*, the constituent for the formation of blood vessel flexible, the constituent for an arteriosclerosis therapy, the food that contains them further, a remedy, and cosmetics.

[0006]

[Embodiment of the Invention] The active principle of the constituent of this invention An aloe vera (Aloe vera), RAKANKA (Momordica grosvenorii), TOCHUU (Eucommia ulmoides), MAKKA (Lepidium yunnanense), oats (Avena sativa), ERUKAMBURI (Gentiana alba), Karkade (Hibiscus sabdariffa), A dill (Anethum graveolens), Calendula officinalis (Calendula officinalis), RYUUGANNIKU (Euphorbia longana), a fennel (Foeniculum vulgare), Tea (Thea sinensis), a peignee royal mint (Mentha pulegium), NETORU (Uraria thunbergiana), areca (Areca catechu), They are a buckwheat (Fagopyrum tartaricum), cube gambir (Uncaria gambir), and the vegetation chosen from department of Combretaceae vegetable TAMI nari R JUNA (Terminalia arjuna).

[0007] All parts of the above-mentioned vegetation, such as the roots, such as terrestrial parts, such as a leaf, a stem, a bud, a flower, cignin, and the bark section (bark), and a root, and a tuber, a seed, fruits, and resin, are usable. Moreover, vegetation contains all for the extract fraction which refined gradually the crude extract by organic solvents, such as the dry matter which dried the vegetation itself, its grinding object, juice obtained by carrying out the squeezing extract of these selves, water or alcohol, the ether, and an acetone, and the crude extract with liquid-liquid distribution, a column chromatography, etc., and was obtained. These may be used independently, and two or more sorts may be mixed and they may be used.

[0008] For example, ethanol 3L is added to 1kg of plant body dry matters of RYUUGANNIKU. The constituent for a skin wrinkling improvement which has a hyaluronic acid are recording acceleration operation for the extract obtained by being immersed at a room temperature overnight as it is, The constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, You may use it as the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, and a constituent for an arteriosclerosis therapy, and the refined thing may be used combining liquid-liquid distribution and various chromatographies.

[0009] That a specific aforementioned vegetable dry matter or an aforementioned specific vegetable extract has a hyaluronic acid are recording acceleration operation is the new knowledge which was not known at all from the former but was acquired by this invention. Hyaluronic acid is known as a biogenic substance which shows very high water retention capacity and viscoelasticity. You may say that hyaluronic acid does not almost have existing independently in a living body, hyaluronic acid tie molecules, such as a protein which has various hyaluronic acid avidity, join together, and the unique matrix is built. This hyaluronic acid rich matrix is found out in most by the part to which an active metabolic turnover change and cell proliferation are seen.

[0010] Hyaluronic acid can be used in order to prevent desiccation of the skin and to maintain the fresh skin according to the outstanding water retention capacity. Although the skin is an organization which has hyaluronic acid in abundance, depolymerize of the hyaluronic acid is carried out with aging, and the water retention capacity declines. Then, aging of the skin can be prevented by holding the hyaluronic acid of the skin to abundance.

[0011] By promoting the amount of production of hyaluronic acid, the failure and symptoms which are generated in the organization of the blood vessel produced by reduction of the amount of production of hyaluronic acid, a joint, an eyeball, etc. are improvable. Moreover, thrombosis can be checked by promoting the production of hyaluronic acid which has thrombosis inhibitory action.

[0012] \*\* of this invention has hyaluronic acid cumulation, and is usable as the constituent for a skin wrinkling improvement, the constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, the constituent for an arteriosclerosis therapy and the food containing these, a remedy, and cosmetics.

[0013] \*\* of this invention can be used and the constituent for a skin wrinkling improvement, the constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, the constituent for an arteriosclerosis therapy and the food containing these, a remedy, and cosmetics can be manufactured.



[0014] The constituent for a skin wrinkling improvement of this invention, the constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, and the constituent for an arteriosclerosis therapy are applicable as food, a remedy, and cosmetics suitably. In the application as a remedy, either internal use or parenteral administration is employable. An active principle can be mixed with the avirulent support for remedies of the solid-state suitable for medication methods, such as internal use, dermal administration, intrarectal administration, and injection, or a liquid on the occasion of the administration as a remedy, and a medicine can be prescribed for the patient with the gestalt of the remedy pharmaceutical preparation of common use. As such pharmaceutical preparation, liquids and solutions, such as solid preparations, such as a tablet, a granule, powder, and a capsule, a solution agent, suspension, and an emulsion, lyophilized products, etc. are mentioned, and these pharmaceutical preparation can be prepared by the stock-in-trade on pharmaceutical preparation, for example. As the above-mentioned avirulent support for remedies, a glucose, a lactose, cane sugar, starch, a mannitol, a dextrin, a fatty-acid glyceride, polyethylene glucoside, hydroxyethylated starch, ethylene glycol, polyoxyethylene sorbitan fatty acid ester, amino acid, gelatin, albumin, water, a physiological saline, etc. are mentioned, for example. Moreover, additives of common use, such as a stabilizing agent, a wetting agent, an emulsifier, a binder, and an isotonicizing agent, can also be added suitably if needed.

[0015] As food, you add nutrition components remaining as it is or various, or make it contain in an eating-and-drinking article, and it can eat as the useful food for health, or a food raw material to a skin wrinkling improvement agent, a skin moisturizer, skin aging preventive, a thrombosis inhibitor, an arthritis therapy agent, a rheumatism therapy agent, dry eye preventive, a blood vessel flexible-sized agent, and an arteriosclerosis therapy agent. For example, the gestalt which was suitable for edible using the means of common use after adding the suitable assistant mentioned above, For example, it may fabricate to granularity, a grain, a tablet, a capsule, a paste, etc., and you may present edible. Moreover, it may be added and used for seafood processing food, such as meat-processing food, such as various food, for example, a ham, and a sausage, boiled fish paste, and a fishcake tube, a pan, confectionery, butter, milk powder, and a fermented milk product, or you may add and use it for drinks, such as water, fruit juice, cow's milk, a soft drink, and tea.

[0016] Although it sets to this invention and the effective dose of active principle slack vegetation is suitably chosen and determined by the strength of a patient's age, weight, a symptom, a patient's extent, a route of administration, an administration schedule, formulation, and the inhibition activity of a raw material etc. For example, in internal use, in the case of per [ 0.001 ] day - 1000 mg/kg extent, and the ethanol extract of an aloe vera, generally, it considers per [ 10 ] day - as 200 mg/kg extent, and a medicine may be prescribed for the patient in several steps on the 1st.

[0017] Moreover, when making \*\* of this invention contain and using it as hyaluronic acid are recording accelerator content cosmetics or a cosmetics raw material, the dry matter or extract of oats can be added in a wheat germ oil or olive oil, and it can be used as a cosmetics raw material. If especially the addition of the dry matter of the vegetation in this invention or an extract is raised as an example, 50 or less % of the weight 0.5 % of the weight or more is suitable for it, although it is not limited 60 or less % of the weight 0.1 % of the weight or more preferably to the weight of a wheat germ oil or olive oil.

[0018] Moreover, the cosmetics which used the aforementioned hyaluronic acid are recording accelerator as a cosmetics component directly can be manufactured. Although not limited especially as cosmetics which made the hyaluronic acid are recording accelerator obtained by the approach of this invention contain, from a functional side, a milky lotion, makeup liquid, a face cream, a hand cream, a lotion, essence, a shampoo, a rinse, etc. are desirable. Such cosmetics can be manufactured according to a conventional method. Although it is not limited, if especially the addition of the dry matter of the vegetation which is an active principle in cosmetics, or an extract is raised as an example, 0.01-% of the weight or more 20 or less % of the weight extent of all cosmetics weight is suitable for it.

[0019] Since the vegetation which is the active principle of this invention was a natural product, even if the toxicity was low, for example, it continued every day at the long period of time of 1000 mg/kg and 100 days and administered the ethanol extract of a fennel orally to the rat, the example of death was not accepted and weight change was not observed, either.

[0020]

[Example] Although an example is given to below and explained concretely, this invention is not limited to these. An examples 1-17 [vegetable extract] aloe vera, RAKANKA, TOCHUU, MAKU, oats, ERUKAMBURI, Karkade, a

dill, Calendula officinalis, RYUUGANNIKU, a fennel, tea, a peignee royal mint, NETORU, areca, a buckwheat, cube gambir, department vegetation of Combretaceae Ethanol 100mL was added to Terminalia arjuna and 20g each, and ethanol was distilled off after carrying out a heating extract for 20 minutes by 50 degrees C and 1500P.S.I. 1350, 3760, 3980, 1670, 1090, 2340, 2100, 2870, 3850, 3210, 3990, 2860, 3460, 2650, 2850, 1890, and 3560 or 2870mg were obtained in order of [ above-mentioned ] the publication as each ethanol extract dry matter, respectively.

#### [0021] [Pharmacological test]

The hyaluronic acid are recording accelerated test hyaluronic acid are recording acceleration operation referred to the trial (biochemistry 73 (2), 429-438 (2001)) which used formalin fixation erythrocyte suspension, and built and evaluated the improving method. That is, after making Homo sapiens fibrocyte cultivate on the plate for tissue culture, the vegetable extract prepared by the above was made to act by the concentration of 5 mg/mL for 16 hours. After removing a culture medium, anion nature colloidal particle suspension 50 and L of the concentration of 2.3 mg/mL (HORUBEN, 843 PERMANENT GREEN DEEP) were added, the field eliminated by the hyaluronic acid rich matrix of a cell was observed under the microscope, and activity was judged in viewing. The assessment result of a hyaluronic acid are recording acceleration operation of each vegetable extract was shown in a table 1. in addition, a criterion -- \*\*= abatement area -- some -- an increment, the increment in O=, and O= -- it expressed with the increment notably.

[0022] The aloe vera which is the vegetation of this invention as a table 1 showed, RAKANKA, TOCHUU, MAKa, oats, ERUKAMBURI, Karkade, a dill, Calendula officinalis, RYUUGANNIKU, a fennel, tea, a peignee royal mint, NETORU, areca, a buckwheat, cube gambir, department vegetation of Combretaceae It turns out that Terminalia arjuna shows a hyaluronic acid are recording acceleration operation.

#### [0023]

##### [A table 1]

表1. 各エタノール抽出エキスのヒアルロン酸蓄積促進作用

	和 名	学 名	作 用
実施例 1	アロエベラ	Aloe vera	◎
実施例 2	ラカンカ	Momordica grosvenorii	□
実施例 3	トチュウ	Eucommia ulmoides	○
実施例 3	マカ	Lepidiummee yenii	□
実施例 4	エンバク	Avena sativa	□
実施例 5	エルカンブリ	Gentianella alboroccea	□
実施例 6	カルカデ	Hibiscus sabdariffa	□
実施例 7	ディル	Anethum graveolenns	□
実施例 8	トウキンセンカ	Calendula officinalis	□
実施例 9	リュウガンニク	Euphoria longana	◎
実施例 10	フェンネル	Foeniculum vulgare	○
実施例 11	チャ	Thea sinensis	□
実施例 12	ペニーロイヤルミント	Mentha pulegium	○
実施例 13	ネトル	Urtrica thunbergiana	□
実施例 14	ピンロウジ	Areca catechu	□
実施例 15	ダッタンソバ	Fagopyrum tartaricum	○
実施例 16	アセンヤク	Uncaria gambir	□
実施例 17	シクンシ科植物	Terminalia arjuna	□

[0024] According to the conventional method, the tablet of the following presentation was manufactured using the ethanol extract of NETORU obtained in the example 1 [manufacture of tablet] example 13 of a formula.

(Group \*\*) (combination: % of the weight)

NETORU extract 24 Lactose 63 Corn starch 12 Cyamoposis Gum 1 [0025] According to the conventional method, the juice of the following presentation was manufactured using the ethanol extract of RAKANKA



obtained in the example 2 [manufacture of juice] example 2 of a formula.

(Group \*\*) (combination: % of the weight)

Frozen concentration Wenzhou mandarin orange fruit juice 5.0 Fruit-sugar grape-sugar liquid sugar 11.0 A citric acid 0.2 L-ascorbic acid 0.02 Perfume 0.2 Coloring matter 0.1 RAKANKA extract 0.2 Water 83.28 [0026]

According to the conventional method, the face cream of the following presentation was manufactured using the ethanol extract of Karkade obtained in the example 3 [manufacture of face cream] example 6 of a formula.

(Group \*\*) (combination: % of the weight)

Isostearic acid isopropyl 8.0 Jojoba oil 6.0 Cetanol 8.0 Stearyl alcohol 2.0 The polyoxyethylene lauryl ether 1.5 Propylene glycol 6.0 Sorbitol 1.0 paraben 0.4 Karkade extract 0.5 vitamin E 0.5 Perfume 0.1 purified water 66.0 [0027]

[Effect of the Invention] The vegetation of this invention is effective in the skin wrinkling improvement which has a hyaluronic acid are recording acceleration operation, the increment in skin moistness, skin aging prevention, thrombosis inhibition, an arthritis therapy, a rheumatism therapy, a dry eye therapy, the formation of blood vessel flexible, and an arteriosclerosis therapy.

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[Translation done.]

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2. \*\*\*\* shows the word which can not be translated.
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**TECHNICAL FIELD**

[The technical field to which invention belongs] This invention relates to the food, the remedy, and cosmetics which show effectiveness to the skin wrinkling improvement with safety high further very, the increment in skin moistness, skin aging prevention, thrombosis inhibition, an arthritis therapy, a rheumatism therapy, a dry eye therapy, the formation of blood vessel flexible, an arteriosclerosis therapy, etc. in relation to an are recording acceleration operation of hyaluronic acid.

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**PRIOR ART**

[Description of the Prior Art] Hyaluronic acid is a kind of the GURIKOSAMINO glucan with which beta-D-N-acetylglucosamine and beta-D-glucuronic acid are the macromolecule polysaccharides of the shape of a straight chain combined by turns, and are widely distributed over connective tissue, such as the skin of mammalian, a blood vessel, a joint, and an eyeball vitreous body. As a function in each organization of hyaluronic acid, it is participating in the resistance to mechanical failures, such as maintenance of the lubricity of an organization, flexibility, and a cell, and external force, etc. deeply with the collagen from the height of the high moisture maintenance capacity, viscoelasticity, or affinity. The amount of production of the hyaluronic acid in each organization decreases with aging, makes the start the skin in which hyaluronic acid exists mostly as the result, and it is said that various kinds of failures and symptoms in an organization of a blood vessel, a joint, an eyeball, etc. occur. Moreover, thrombosis inhibitory action is also reported to hyaluronic acid (Artery19 (5), 256-270 (1992)), and having an improvement operation also in the blood circulatory system besides to the failure and symptoms which are generated in each above-mentioned organization an improvement operation is known by promoting the amount of production.

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**EFFECT OF THE INVENTION**

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**TECHNICAL PROBLEM**

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MEANS

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[0013] \*\* of this invention can be used and the constituent for a skin wrinkling improvement, the constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, the constituent for an arteriosclerosis therapy and the food containing these, a remedy, and cosmetics can be manufactured.

[0014] The constituent for a skin wrinkling improvement of this invention, the constituent for skin moisturization, the constituent for skin aging prevention, the constituent for thrombosis inhibition, the constituent for an arthritis therapy, the constituent for a rheumatism therapy, the constituent for dry eye prevention, the constituent for the formation of blood vessel flexible, and the constituent for an arteriosclerosis therapy are applicable as food, a remedy, and cosmetics suitably. In the application as a remedy, either internal use or parenteral administration is employable. An active principle can be mixed with the avirulent support for remedies of the solid-state suitable for medication methods, such as internal use, dermal administration, intrarectal administration, and injection, or a liquid on the occasion of the administration as a remedy, and a medicine can be prescribed for the patient with the gestalt of the remedy pharmaceutical preparation of common use. As such pharmaceutical preparation, liquids and solutions, such as solid preparations, such as a tablet, a granule, powder, and a capsule, a solution agent, suspension, and an emulsion, lyophilized products, etc. are mentioned, and these pharmaceutical preparation can be prepared by the stock-in-trade on pharmaceutical preparation, for example. As the above-mentioned avirulent support for remedies, a glucose, a lactose, cane sugar, starch, a mannitol, a dextrin, a fatty-acid glyceride, polyethylene glucol, hydroxyethylated starch, ethylene glycol, polyoxyethylene sorbitan fatty acid ester, amino acid, gelatin, albumin, water, a physiological saline, etc. are mentioned, for example. Moreover, additives of common use, such as a stabilizing agent, a wetting agent, an emulsifier, a binder, and an isotoning agent, can also be added suitably if needed.

[0015] As food, you add nutrition components remaining as it is or various, or make it contain in an eating-and-drinking article, and it can eat as the useful food for health, or a food raw material to a skin wrinkling improvement agent, a skin moisturizer, skin aging preventive, a thrombosis inhibitor, an arthritis therapy agent, a rheumatism therapy agent, dry eye preventive, a blood vessel flexible-ized agent, and an arteriosclerosis therapy agent. For example, the gestalt which was suitable for edible using the means of common use after adding the suitable assistant mentioned above, For example, it may fabricate to granularity, a grain, a tablet, a capsule, a paste, etc., and you may present edible. Moreover, it may be added and used for seafood processing food, such as meat-processing food, such as various food, for example, a hum, and a sausage, boiled fish paste, and a fishcake tube, a pan, confectionery, butter, milk powder, and a fermented milk product, or you may add and use it for drinks, such as water, fruit juice, cow's milk, a soft drink, and tea.

[0016] Although it sets to this invention and the effective dose of active principle slack vegetation is suitably chosen and determined by the strength of a patient's age, weight, a symptom, a patient's extent, a route of administration, an administration schedule, formulation, and the inhibition activity of a raw material etc. For example, in internal use, in the case of per [ 0.001 ] day - 1000 mg/kg extent, and the ethanol extract of an aloe vera, generally, it considers per [ 10 ] day - as 200 mg/kg extent, and a medicine may be prescribed for the patient in several steps on the 1st.

[0017] Moreover, when making \*\* of this invention contain and using it as hyaluronic acid are recording accelerator content cosmetics or a cosmetics raw material, the dry matter or extract of oats can be added in a wheat germ oil or olive oil, and it can be used as a cosmetics raw material. If especially the addition of the dry matter of the vegetation in this invention or an extract is raised as an example, 50 or less % of the weight 0.5 % of the weight or more is suitable for it, although it is not limited 60 or less % of the weight 0.1 % of the weight or

more preferably to the weight of a wheat germ oil or olive oil.

[0018] Moreover, the cosmetics which used the aforementioned hyaluronic acid are recording accelerator as a cosmetics component directly can be manufactured. Although not limited especially as cosmetics which made the hyaluronic acid are recording accelerator obtained by the approach of this invention contain, from a functional side, a milky lotion, makeup liquid, a face cream, a hand cream, a lotion, essence, a shampoo, a rinse, etc. are desirable. Such cosmetics can be manufactured according to a conventional method. Although it is not limited, if especially the addition of the dry matter of the vegetation which is an active principle in cosmetics, or an extract is raised as an example, 0.01-% of the weight or more 20 or less % of the weight extent of all cosmetics weight is suitable for it.

[0019] Since the vegetation which is the active principle of this invention was a natural product, even if the toxicity was low, for example, it continued every day at the long period of time of 1000 mg/kg and 100 days and administered the ethanol extract of a fennel orally to the rat, the example of death was not accepted and weight change was not observed, either.

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[Translation done.]



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1. This document has been translated by computer. So the translation may not reflect the original precisely.
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3. In the drawings, any words are not translated.

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EXAMPLE

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[Example] Although an example is given to below and explained concretely, this invention is not limited to these. An examples 1-17 [vegetable extract] aloe vera, RAKANKA, TOCHUU, MAKAKA, oats, ERUKAMBURI, Karkade, a dill, Calendula officinalis, RYUUGANNIKU, a fennel, tea, a peignee royal mint, NETORU, areca, a buckwheat, cube gambir, department vegetation of Combretaceae Ethanol 100mL was added to Terminalia arjuna and 20g each, and ethanol was distilled off after carrying out a heating extract for 20 minutes by 50 degrees C and 1500P.S.I. 1350, 3760, 3980, 1670, 1090, 2340, 2100, 2870, 3850, 3210, 3990, 2860, 3460, 2650, 2850, 1890, and 3560 or 2870mg were obtained in order of [ above-mentioned ] the publication as each ethanol extract dry matter, respectively.

[0021] [Pharmacological test]

The hyaluronic acid are recording accelerated test hyaluronic acid are recording acceleration operation referred to the trial (biochemistry 73 (2), 429-438 (2001)) which used formalin fixation erythrocyte suspension, and built and evaluated the improving method. That is, after making Homo sapiens fibrocyte cultivate on the plate for tissue culture, the vegetable extract prepared by the above was made to act by the concentration of 5 mg/mL for 16 hours. After removing a culture medium, anion nature colloidal particle suspension 50 and L of the concentration of 2.3 mg/mL (HORUBEN, 843 PERMANENT GREEN DEEP) were added, the field eliminated by the hyaluronic acid rich matrix of a cell was observed under the microscope, and activity was judged in viewing. The assessment result of a hyaluronic acid are recording acceleration operation of each vegetable extract was shown in a table 1. in addition, a criterion -- \*\*= abatement area -- some -- an increment, the increment in O=, and O= -- it expressed with the increment notably.

[0022] The aloe vera which is the vegetation of this invention as a table 1 showed, RAKANKA, TOCHUU, MAKAKA, oats, ERUKAMBURI, Karkade, a dill, Calendula officinalis, RYUUGANNIKU, a fennel, tea, a peignee royal mint, NETORU, areca, a buckwheat, cube gambir, department vegetation of Combretaceae It turns out that Terminalia arjuna shows a hyaluronic acid are recording acceleration operation.

[0023]

[A table 1]

表1. 各エタノール抽出エキスのヒアルロン酸蓄積促進作用

	和 名	学 名	作 用
実施例1	アロエベラ	<i>Aloe vera</i>	◎
実施例2	ラカンカ	<i>Momordica grosvenorii</i>	□
実施例3	トチュウ	<i>Eucommia ulmoides</i>	○
実施例3	マカ	<i>Lepidiummee yenil</i>	□
実施例4	エンバク	<i>Avena sativa</i>	□
実施例5	エルカンブリ	<i>Gentianella alboroccea</i>	□
実施例6	カルカデ	<i>Hibiscus sabdariffa</i>	□
実施例7	ディル	<i>Anethum graveolenns</i>	□
実施例8	トウキンセンカ	<i>Calendula officinalis</i>	□
実施例9	リュウガンニク	<i>Euphoria longana</i>	◎
実施例10	フェンネル	<i>Foeniculum vulgare</i>	○
実施例11	チャ	<i>Thea sinensis</i>	□
実施例12	ペニーロイヤルミント	<i>Mentha pulegium</i>	○
実施例13	ネトル	<i>Urtrica thunbergiana</i>	□
実施例14	ビンロウジ	<i>Areca catechu</i>	□
実施例15	ダッタンソバ	<i>Fagopyrum tartaricum</i>	○
実施例16	アセンヤク	<i>Uncaria gambir</i>	□
実施例17	シクンシ科植物	<i>Terminalia arjuna</i>	□

[0024] According to the conventional method, the tablet of the following presentation was manufactured using the ethanol extract of NETORU obtained in the example 1 [manufacture of tablet] example 13 of a formula.

(Group \*\*) (combination: % of the weight)

NETORU extract 24 Lactose 63 Corn starch 12 Cyamoposis Gum 1 [0025] According to the conventional method, the juice of the following presentation was manufactured using the ethanol extract of RAKANKA obtained in the example 2 [manufacture of juice] example 2 of a formula.

(Group \*\*) (combination: % of the weight)

Frozen concentration Wenzhou mandarin orange fruit juice 5.0 Fruit-sugar grape-sugar liquid sugar 11.0 A citric acid 0.2 L-ascorbic acid 0.02 Perfume 0.2 Coloring matter 0.1 RAKANKA extract 0.2 Water 83.28 [0026]

According to the conventional method, the face cream of the following presentation was manufactured using the ethanol extract of Karkade obtained in the example 3 [manufacture of face cream] example 6 of a formula.

(Group \*\*) (combination: % of the weight)

Isostearic acid isopropyl 8.0 Jojoba oil 6.0 Cetanol 8.0 Stearyl alcohol 2.0 The polyoxyethylene lauryl ether 1.5 Propylene glycol 6.0 Sorbitol 1.0 paraben 0.4 Karkade extract 0.5 vitamin E 0.5 Perfume 0.1 purified water 66.0

[Translation done.]